

## REMARKS

The Examiner rejected claims 1-38. Claims 2, 3, 6, 8, 9, 11, 13-16, 18, 25, 27-34, and 37 have been cancelled without prejudice. Thus, claims 1, 4, 5, 7, 10, 12, 17, 19-24, 26, 35, 36, and 38 are pending.

Claims 1, 4, 5, 7, 10, 12, 17, 19-24, 26, 35, 36, and 38 have been amended. For example, each independent claim has been amended to indicate that the recited recombinant nucleic acid comprises a nucleotide sequence encoding an autocatalytically cleaving ribozyme and a trans-acting ribozyme, wherein the nucleotide sequence is operably linked to a promoter with the proviso that the promoter is not a target-specific promoter that targets bacteria, wherein the autocatalytically cleaving ribozyme comprises a first arm of complementary sequence and a second arm of complementary sequence, wherein the cleavage site of the autocatalytically cleaving ribozyme is located between the first and second arms, and wherein one of the first and second arms is proximal to the trans-acting ribozyme, and the other of the first and second arms is longer than the corresponding arm of a pCLIP cassette.

Applicants' specification fully supports these amendments. For example, page 13, lines 20-21 and Figure 3 of Applicants' specification disclose a nucleotide sequence encoding autocatalytically cleaving ribozymes and a trans-acting ribozyme, wherein each autocatalytically cleaving ribozyme comprises a first arm of complementary sequence and a second arm of complementary sequence with one of the first and second arms being proximal to the trans-acting ribozyme, and the other of the first and second arms being longer than the corresponding arm of a pCLIP cassette. In addition, page 36, lines 7-8 disclose lengthening the arms of cis-acting ribozymes. Further, the section extending from page 18, line 31 to page 19, line 16 discloses expression vectors for procaryotic and eucaryotic expression, while page 38, lines 12-14 disclose that a promoter can target bacteria, fungi, yeasts, parasites, viruses, or non-viral pathogens. Thus, no new matter has been added.

In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 1, 4, 5, 7, 10, 12, 17, 19-24, 26, 35, 36, and 38.

### Information Disclosure Statement

Applicants respectfully note that an initialed copy of the PTO-1449 form filed November 1, 2002 has not been returned. Thus, Applicants respectfully request return of an initialed copy. For the Examiner's convenience, a copy of the PTO-1449 form filed November 1, 2002 is attached hereto. In addition, copies of the listed references can be resubmitted upon request.

### Double Patenting Rejections

The Examiner rejected claims 1-24 and 26-38 under the judicially created doctrine of double patenting over claims 1-5 of U.S. Patent No. 5,824,519. The Examiner alleges that the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

Applicants respectfully disagree. To further prosecution, however, claims 2, 3, 6, 8, 9, 11, 13-16, 18, 27-34, and 37 have been cancelled without prejudice. In addition, independent claims 1, 10, 12, and 17 have been amended to indicate that the recited autocatalytically cleaving ribozyme comprises a first arm of complementary sequence and a second arm of complementary sequence, wherein the cleavage site of the autocatalytically cleaving ribozyme is located between the first and second arms, and wherein one of the first and second arms is proximal to the trans-acting ribozyme, and the other of the first and second arms is longer than the corresponding arm of a pCLIP cassette.

Claims 1-5 of U.S. Patent No. 5,824,519 do not recite a recombinant nucleic acid comprising such a nucleotide sequence. In fact, at no point do the claims 1-5 of U.S. Patent No. 5,824,519 teach or suggest a nucleotide sequence encoding an autocatalytically cleaving ribozyme comprising a first arm of complementary sequence and a second arm of complementary sequence, wherein the cleavage site of the autocatalytically cleaving ribozyme is located between the first and second arms, and wherein one of the first and second arms is proximal to the trans-acting ribozyme, and the other of the first and second arms is longer than the corresponding arm of a pCLIP cassette. Thus, the presently amended claims are patentably distinct from claims 1-5 of U.S. Patent No. 5,824,519.

In light of the above, Applicants respectfully request withdrawal of the double patenting rejection of claims 1, 4, 5, 7, 10, 12, 17, 19-24, 26, 35, 36, and 38.

The Examiner also rejected claims 1-16 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,271,359.

Applicants respectfully disagree. To further prosecution, however, claims 2, 3, 6, 8, 9, 11, and 13-16 have been cancelled without prejudice. In addition, independent claims 1, 10, and 12 have been amended to indicate that the recited autocatalytically cleaving ribozyme comprises a first arm of complementary sequence and a second arm of complementary sequence, wherein the cleavage site of the autocatalytically cleaving ribozyme is located between the first and second arms, and wherein one of the first and second arms is proximal to the trans-acting ribozyme, and the other of the first and second arms is longer than the corresponding arm of a pCLIP cassette.

Claims 1-7 of U.S. Patent No. 6,271,359 do not recite a recombinant nucleic acid comprising such a nucleotide sequence. In fact, at no point do the claims 1-7 of U.S. Patent No. 6,271,359 teach or suggest a nucleotide sequence encoding an autocatalytically cleaving ribozyme comprising a first arm of complementary sequence and a second arm of complementary sequence, wherein the cleavage site of the autocatalytically cleaving ribozyme is located between the first and second arms, and wherein one of the first and second arms is proximal to the trans-acting ribozyme, and the other of the first and second arms is longer than the corresponding arm of a pCLIP cassette. Thus, the presently amended claims are patentably distinct from claims 1-7 of U.S. Patent No. 6,271,359.

In light of the above, Applicants respectfully request withdrawal of the double patenting rejection of claims 1, 4, 5, 7, 10, and 12.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 28, 30, and 32 under 35 U.S.C. § 112, second paragraph, as being indefinite, stating that these claims lack sufficient antecedent basis.

Claims 28, 30, and 32 have been cancelled without prejudice. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 27-32 under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants respectfully disagree. To further prosecution, however, claims 27-32 have been cancelled without prejudice. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 102(e)

The Examiner rejected claims 1-3, 6, 7, 10, 11, 17, and 18 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,824,519. The Examiner alleges that U.S. Patent No. 5,824,519 teaches each and every aspect of the claimed invention thereby anticipating claims 1-3, 6, 7, 10, 11, 17, and 18.

Applicants respectfully disagree. To further prosecution, however, claims 2, 3, 6, 11, and 18 have been cancelled without prejudice. In addition, independent claims 1, 10, 12, and 17 have been amended to indicate that the recited autocatalytically cleaving ribozyme comprises a first arm of complementary sequence and a second arm of complementary sequence, wherein the cleavage site of the autocatalytically cleaving ribozyme is located between the first and second arms, and wherein one of the first and second arms is proximal to the trans-acting ribozyme, and the other of the first and second arms is longer than the corresponding arm of a pCLIP cassette.

At no point does U.S. Patent No. 5,824,519 disclose an autocatalytically cleaving ribozyme comprising a first arm of complementary sequence and a second arm of

complementary sequence, wherein one of the arms is proximal to a trans-acting ribozyme, and the other arm is longer than the corresponding arm of a pCLIP cassette. Thus, U.S. Patent No. 5,824,519 does not anticipate the presently amended claims.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 7, 10, and 17 under 35 U.S.C. § 102(e).

Rejections under 35 U.S.C. § 102(a)

The Examiner rejected claims 1-26 and 33-38 under 35 U.S.C. § 102(a) as being anticipated by the Norris *et al.* reference (WO 98/24925). The Examiner alleges that the Norris *et al.* reference teaches each and every aspect of the claimed invention, thereby anticipating claims 1-26 and 33-38.

Applicants respectfully disagree. To further prosecution, however, claims 2, 3, 6, 8, 9, 11, 13-16, 18, 25, 33, 34, and 37 have been cancelled without prejudice. With respect to claims 1, 4, 5, 7, 10, 12, 17, 19-24, 26, 35, 36, and 38, Applicants respectfully submit that the accompanying declaration filed under 37 C.F.R. §1.132 demonstrates that the Norris *et al.* reference is the inventors' own work.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 4, 5, 7, 10, 12, 17, 19-24, 26, 35, 36, and 38 under 35 U.S.C. §102(a).

Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-24 and 33-38 under 35 U.S.C. § 103(a) as being unpatentable over the Taira *et al.* reference (U.S. Patent No. 5,500,357) or the Ruiz *et al.* reference (U.S. Patent No. 5,912,149) in view of the Ohta *et al.* reference (*Nucleic Acids Research*, Vol. 24, No. 5, pages 938-942 (1996)). Specifically, the Examiner alleged that the Taira *et al.* reference teaches a plasmid encoding genes inserted between 5' and 3' self-cleavage ribozymes but does not disclose the use of tissue-specific or pathogenic specific promoters in the plasmid. The Examiner further alleged that the Ohta *et al.* reference discloses the use of tissue-specific promoters in recombinant plasmids encoding trans-activating ribozymes. The Examiner thus concluded that a person having ordinary skill in the art would have been motivated to design recombinant nucleic acid sequences comprising nucleotide sequences encoding self-cleaving ribozymes and one or more trans-acting ribozymes operably linked to a tissue-specific or pathogen-specific promoter.

Applicants respectfully disagree. To further prosecution, however, claims 2, 3, 6, 8, 9, 11, 13-16, 18, 33, 34, and 37 have been cancelled without prejudice. In addition, independent claims 1, 10, 12, and 17 have been amended to indicate that the recited autocatalytically cleaving ribozyme comprises a first arm of complementary sequence and a second arm of complementary sequence, wherein the cleavage site of the autocatalytically cleaving ribozyme is located between the first and second arms, and wherein one of the first and second arms is proximal to the trans-acting ribozyme, and the other of the first and second arms is longer than the corresponding arm of a pCLIP cassette.

The Taira *et al.* reference discloses recombinant plasmids encoding genes inserted between 5' and 3' self-cleaving ribozymes. The Ruiz *et al.* reference discloses multimeric self-cleaving ribozymes. At no point do these reference disclose an autocatalytically cleaving ribozyme that has a first arm of complementary sequence and a second arm of complementary sequence with one of the arms being proximal to a trans-acting ribozyme and the other being longer than the corresponding arm of a pCLIP cassette. In fact, the cited references do not provide any suggestion that a person having ordinary skill in the art should make or use an autocatalytically cleaving ribozyme with an arm longer than a corresponding arm of a pCLIP cassette.

The Ohta *et al.* reference fails to correct the deficiencies of the Taira *et al.* and Ruiz *et al.* references. In fact, the Ohta *et al.* reference merely discloses the tissue-specific expression of an anti-ras ribozyme using a tyrosinase promoter. Thus, a person having ordinary skill in the art reading the cited references would not have been motivated to make or use the presently claimed invention.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 4, 5, 7, 10, 12, 17, 19-24, 35, 36, and 38 under 35 U.S.C. § 103(a).



Applicant : James S. Norris et al.  
Serial No. : 10/082,973  
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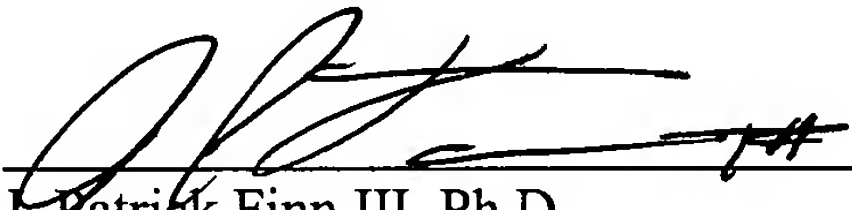
Attorney's Docket No.: 14017-004002 / PSU 96-1566

### CONCLUSION

Applicants submit that claims 1, 4, 5, 7, 10, 12, 17, 19-24, 26, 35, 36, and 38 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned agent at the telephone number below if such will advance prosecution of this application. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.

Respectfully submitted,

Date: March 17, 2004

  
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J. Patrick Finn III, Ph.D.  
Reg. No. 44,109

Fish & Richardson P.C., P.A.  
60 South Sixth Street, Suite 3300  
Minneapolis, MN 55402  
Telephone: (612) 335-5070  
Facsimile: (612) 288-9696